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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	

ART UNIT	PAPER NUMBER
	11

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/485,245	Applicant(s) Hopkins, A
	Examiner CB Wilder	Group Art Unit 1655

X Responsive to communication(s) filed on *Jan 26, 2001* .

This action is **FINAL.**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) *1-6* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

X Claim(s) *1-6* is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

X The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

X Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

X All Some* None of the CERTIFIED copies of the priority documents have been

X received.

received in Application No. (Series Code/Serial Number) _____ .

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

1. Applicant's amendment filed January 26, 2001 in Paper No. 10 is acknowledged. claims 2, 5 and 6 have been amended. Claims 1-6 are pending. The arguments have been thoroughly reviewed but they are not found persuasive for the reasons that follows. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims.

2. The text of those sections pf title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Objections and Rejections

3. The prior objections to the title and specification is withdrawn in view of Applicant's submission of a new title and correction of misspelled words. The claim rejections under 35 U.S.C. 112 second paragraph is withdrawn in view of Applicant's amendment of the claims. The prior art rejection under 35 U.S.C. 102 (a) is withdrawn in view of Applicant's arguments. The prior art rejection under 35 U.S.C. 103(a) is withdrawn in view of Applicant's arguments and amendments of the claims.

New Ground(s) of Rejection

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1- 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suganuma et al. (Analytical Biochemistry January 20, 1995), and further in view of Shen et al (EP 0 726 310 August 14. 1996). Regarding claims 1, 2 and 4, Suganuma et al. also teach a labeling composition comprising a random mixture of oligonucleotides which are 5 mers to 11 mers (page 605, col. 2, lines 36 and 37). Suganuma et al. teach wherein the composition further comprise a polymerase enzyme, a supply of nucleotides for chain extension, a labeled nucleotide and buffer (page 606, lines 1-10). The composition Suganuma et al. differ from that of the claimed invention in that the references do not teach wherein a dye and/or stabilizer is added to the composition. In a composition similar to that of Suganuma et al., Shen et al. teach wherein the composition is present in a dry state. Shen et al. also teach wherein the composition comprise a stabilizer along with a polymerase enzyme and a supply of nucleotides for chain extension (page 6, lines 3-7 and 22). Shen et al. do not expressly teach the incorporation of a dye. However, the use of dyes as labeling agents was routinely practiced in the art. It would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to add a stabilizer to the labeling composition of Suganuma et al.. One of ordinary skill in the art would have been motivated to do for the expected benefits taught by Shen et al. that a stabilizing agent prevents or delays the loss of a composition's biological activity as a result of storage over time (page 4, lines 8-10). One of ordinary skill in the art would have been motivated further to add a dye for labeling in view of routine art practice for the obvious benefit of visualizing a polynucleotide generated with the composition.

Regarding claim 3, Suganuma et al. teach, wherein the random mixture is of 6 mer oligonucleotides (page 605, col. 2, lines 36 and 37).

Regarding claim 5, Suganuma et al. in view of Chen et al. teach a method of making a labeled probe for a nucleic acid template, wherein the method comprises the steps of providing a nucleic acid template and labeling composition and incubating the nucleic acid template under chain extension conditions with the labeling composition (bottom of page 605, beginning at line 38 to page 606, lines 1 1-11).

10. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Suganuma et al. in view of Shen et al. in view of Hoeltke et al. (5,814,502, effective filing date October 1994) and further in view of Strategene (January 1997). Regarding claim 6, Suganuma et al. in view of Shen et al. teach a labeling composition and method of making a labeled probe comprising a number of method steps wherein the labeled compositions comprises a random mixture of oligonucleotides which are 6 mers to 8-mers, and said composition present in a dry state. The labeling composition of the disclosure differs from that of the references in that the references do not expressly teach the concentration of the random mixture of oligonucleotides. However the optimal contents range would have been determined by the practitioner based on desired properties of the random oligonucleotides, desired lengths of the random oligonucleotides and desired results. For example, in a method for labeling nucleic acid, Hoeltke et al. teach a random mixture of oligonucleotides wherein the concentration range of approximately 15 to 80 OD/ml is selected for the various random primers which are 6-mers to 15- mers. Hoeltke et al. further teach that depending on the primer length, the optimal contents range will change (col. 2, lines 55-60 and col. 3, lines 38-42). Strategene teaches

a labeling composition comprising mixture of oligonucleotides which are 7-mers to 8-mers wherein the mixture of oligonucleotides are present at a concentration of about 1 OD/ml to 10 OD/ml. In view of the foregoing, it would have been obvious to one of ordinary skill in the art that the concentration range of the random mixture of oligonucleotide may vary based the practitioner's preference as well as the length of the primers as suggested by Hoeltke et al.

11. Applicant traverses the rejection on the following grounds: Applicant argues each of the references separately and state that the reference do not render obvious the selection of 6, 7, or 8-mers in a dry state. Applicant argues that in fact, Suganuma teaches a away from the unexpected results obtained by the invention by teaching a selection of 5-mers to 11-mers. Applicant states that further Suganuma fails to suggest that the composition be provided in a dry state. Applicant further argues that Shen discloses that the dried formulation contains enzymes cryoprotectant, nucleotide triphosphates, metal ions and cofactors but seems to teach that the dried composition is reconstituted before the addition of the primers. Finally, Applicant argues that while the Examine cites page 6, line 3-6 and 22 in support of the proposition that the composition comprises primers in a dry state there is no indication that the oligonucleotide primer is actually presenting those compositions. Applicant states that the rejection be withdrawn.

12. The arguments have been thoroughly reviewed and considered but they are not found persuasive for the reasons that follows: Firstly, in response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In

this case, the reference of Suganuma provides the limitations of the claimed invention of a labeling composition comprising a random mixture of oligonucleotides which are 6mers- to 8-mers in the teaching of a labeling composition comprising a random mixture of oligonucleotides which are 5mers to 11-mers. Furthermore, as set forth by the court in *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955), "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation". The court has established that "a claim which falls within the broad scope of the references is held unpatentable thereover because, among other reasons, there is no evidence of the **criticality** of the claimed ranges" (See *in re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA)). Therefore, as noted in the prior Office Action, the random mixture of oligonucleotides of the claimed invention falls *within* the range of the random mixture of oligonucleotides of Suganuma. The reference does not teach the composition in a dry state, however this limitation is provided in the reference of Shen et al. Shen et al. teach a composition comprising oligonucleotides in dried state (page 15, Example 6). Shen et al. also teach wherein the composition comprise a stabilizer along with a polymerase enzyme and a supply of nucleotides for chain extension (page 6, lines 3-7 and 22). In response to Applicant argument that Shen appears to teach the dried composition in reconstituted form before the addition of primers, the Examiner disagrees because Shen states that the amplification primers may be included in the freeze-dried composition so as to reduce the number of methods of using such a reagent and to reduce the number of containers in a kit of nucleic acid amplification (page 15, lines 30-32). The arguments are not sufficient to overcome the prior art rejection.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The Examiner can normally be reached on Monday through Thursday from 7:00 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Exr.'s supervisor, W. Gary Jones, can be reached at (703) 308-1152. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed the Group's receptionist whose telephone number is (703) 308-0196.

Cynthia B. Wilder

Cynthia B. Wilder, Ph.D.

March 27, 2001

W. Gary Jones
Supervisory Patent Examiner
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3/30/01